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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/150,813	09/11/98	GRAINGER	D 295.027US1

021186 HM22/1129
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH
P.O. BOX 2938
MINNEAPOLIS MN 55402

EXAMINER	
MURPHY, J	
ART UNIT	**PAPER NUMBER**
1646	16

DATE MAILED: 11/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/150,813	GRAINGER ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *11 September 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,, 20-21, 24-28, 31-35, 41-45, 48-50, 52-62* is/are pending in the application.

4a) Of the above claim(s) *21, 24-28, 31-33, 35, 45, 48-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,20,22,34,41-44 and 52-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claims 1-16, 18-19, 23, 29-30, 36-39, 46-47 and 51 were cancelled, claims 17, 20, 22 and 34 were amended and claims 52-62 were added in Paper No. 14, 9/11/2000.

Claims 17, 20, 22, 34, 41-44 and 52-62 are under consideration.

Response to Amendment

The cancellation of claim 51 in Paper No. 14, 9/11/2000 obviates the rejection under 35 USC § 101, and the rejection is thus withdrawn.

The rejection of pending claims 1-17, 20, 22, 34 and 41-44 under 35 USC § 112, first paragraph for recitation of the term "chemokine peptide 3" has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of pending claims 17, 20, 22, 34, 41-44 under 35 USC § 112, second paragraph for recitation of chemokine peptide 3, has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of pending claims 17, 20, 22, 34 under 35 USC § 102(a) as being anticipated by Gong et al. (1997) has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of pending claims 17, 20, 22 and 34 under 35 USC § 103(a) as being unpatentable over Gong et al. (1995) has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 17 and 41-44 under 35 USC § 103(a) as being unpatentable over Gong et al. (1995) in view of Sozzani et al. (1996) has been obviated by Applicant's amendment, and is thus withdrawn.

The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112 first paragraph

Claims 17, 20, 22, 34, 41-44 and 52-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. V. Makurhar, 19 USPQ2d 1111, makes clear that applicant must convey with reasonable clarity to those skilled in the art, as the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry whatever is now claimed (see page 1117). Due to the limitation of "a variant thereof, a derivative thereof" recited in the claim, a determination of what the claim as a whole covers indicates that elements which are not particularly described, e.g. the sequence of the claimed variants and derivatives, are encompassed by this claim. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath Inc. V. Makurhar, page 1116.). One can not describe what one has not conceived. See Fiddes v. Baird 30 USPQ 2d 1481, 1483.

There is no actual reduction to practice of the claimed invention, or complete detailed description of the structure. A biomolecular sequence described only by a functional characteristic, in this case a variant or derivative of a chemokine, without any known or disclosed correlation between the function and the structure of the sequence is not a sufficient identifying characteristic. See University of California v. Eli Lilly and Co. 43 USPQ2d at 1406. There is no known or disclosed correlation between this function and the structure of the non-described variants and derivatives of a chemokine. Weighing all factors in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed invention.

Claims 17, 20, 22, 34, 41-44, 52-56, 59, 61- 62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preventing dermal inflammation or asthma using CRD-$Leu_4Ile_{11}Cys_{13}$peptide 3(3-12)[MCP-1], it does not reasonably provide enablement for a method of preventing dermal inflammation or asthma using peptides of a peptide of a chemokine, variants thereof or derivatives thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 17, 20, 22 and 34 are overly broad in the recitation of "a peptide of a chemokine, a variant thereof, a derivative thereof " since no guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of a CRD-$Leu_4Ile_{11}Cys_{13}$peptide 3(3-12)[MCP-1],

Applicants disclose that peptides of a chemokine, variants thereof or derivatives thereof comprise no more than 30 peptidyl residues which have at least 50% contiguous amino acid homology or identity to the corresponding native chemokine (page 39, lines 15-20), without disclosing any actual or prophetic examples on expected performance parameters of any of the possible muteins of a chemokine peptide. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of ordinary skill in the art would generate a chemokine peptide variant or derivative other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is

necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. The guidance provided requires only a reasonable amount of experimentation". However, the CAFC decision (Genentech Inc. v. Novo Nordisk, 42 USPQ2d 1001, 1997) expressly states that:

"When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

Given the breadth of claims 17, 20, 22 and 34 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to make and use the claimed invention. Claims 41-44, 52-56, 59 and 61- 62 are rejected due to their dependence on the recitation in claims 17, 20, 22 and 34 of "peptide of a chemokine, a variant thereof, a derivative thereof".

Claims 17, 20, 22, 34, 41-44, 52-56, 59, 61- 62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preventing dermal inflammation or asthma using CRD-$Leu_4Ile_{11}Cys_{13}$peptide 3(3-12)[MCP-1], it does not reasonably provide enablement for a method of preventing or inhibiting an indication associated with a chemokine induced activity using peptides of a peptide of a chemokine, variants thereof or derivatives thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant, in Paper No. 14, 9/11/2000, lists the maladies which are to be considered an indication of a chemokine induced activity. However, these conditions are distinct because the pathological conditions differ in etiologies and therapeutic endpoints. Applicant has not provided any teaching of how to prevent or inhibit any of the listed indications using the claimed method other than the data provided in the dermal inflammation or asthma models in rat or mouse, respectively. Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23

USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). The CAFC decision (Genentech Inc. v. Novo Nordisk, 42 USPQ2d 1001, 1997) expressly states that:

> "When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of claims 17, 20, 22, 34, 41-44, 52-56, 59, 61- 62 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112 second paragraph

Claims 17 and 20 stand rejected under 35 USC § 112, second paragraph for recitation of the term "indication" for reasons of record set forth in Paper No. 11, 2/23/2000. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
November 14, 2000

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER